

## ORIGINAL ARTICLE

## Gray matter anomalies in pedophiles with and without a history of child sexual offending

B Schiffer<sup>1,2,10</sup>, T Amelung<sup>3,10</sup>, A Pohl<sup>4</sup>, C Kaergel<sup>1,2</sup>, G Tenbergen<sup>5</sup>, H Gerwinn<sup>4</sup>, S Mohnke<sup>6</sup>, C Massau<sup>1,2</sup>, W Matthias<sup>5</sup>, S Weiß<sup>2</sup>, V Marr<sup>7,8</sup>, KM Beier<sup>3</sup>, M Walter<sup>7,8</sup>, J Ponseti<sup>4</sup>, THC Krüger<sup>5</sup>, K Schiltz<sup>7,9,10</sup> and H Walter<sup>6,10</sup>

Pedophilia is a psychiatric disorder that is inter-related with but distinct from child sexual offending (CSO). Neural alterations reportedly contribute to both pedophilia and CSO, but until now, no study has distinguished the brain structural anomalies associated with pedophilia from those specifically associated with CSO in pedophilic men. Using high-resolution T1-weighted brain images and voxel-based morphometry, we analyzed the gray matter (GM) volume of the following 219 men recruited at four acquisition sites in Germany: 58 pedophiles with a history of CSO, 60 pedophiles without any history of CSO and 101 non-pedophilic, non-offending controls to control for the effects of age, education level, verbal IQ, sexual orientation and the acquisition site. Although there were no differences in the relative GM volume of the brain specifically associated with pedophilia, statistical parametric maps revealed a highly significant and CSO-related pattern of above vs below the 'normal' GM volume in the right temporal pole, with non-offending pedophiles exhibiting larger volumes than offending pedophiles. Moreover, regression analysis revealed that the lower GM volume of the dorsomedial prefrontal or anterior cingulate cortex was associated with a higher risk of re-offending in pedophilic child molesters. We believe our data provide the first evidence that CSO in pedophilia rather than pedophilia alone is associated with GM anomalies and thus shed new light on the results of previous studies on this topic. These results indicate the need for new neurobehavioral theories on pedophilia and CSO and may be potentially useful for treatment or prevention approaches that aim to reduce the risk of (re)offending in pedophilia.

*Translational Psychiatry* (2017) **7**, e1129; doi:10.1038/tp.2017.96; published online 16 May 2017

## INTRODUCTION

Pedophilia is a disorder of sexual preference (ICD-10) or a paraphilia (DSM-5) that is characterized by sexual impulses, urges and fantasies involving male (attracted to boys) or female (attracted to girls) sexually immature children or children of both sexes. Note that in ICD-10, these definitions include prepubertal and early pubertal children, while the DSM-5 specifically states 'prepubertal children (generally age 13 and younger)'. These interests can occur either exclusively or non-exclusively, that is, in combination with sexual interest in adults. Pedophilia is a diagnosable mental disorder when accompanied by significant distress, social function impairment or harmful behaviors. Although recent population-based studies suggest that the prevalence of pedophilic interest is 1–5% in men, the generalizability of these findings remains questionable.<sup>1</sup> Pedophilia is a major risk factor for committing repeated-contact sexual offenses against children. However, only approximately 50% of convicted child sexual offenders (CSO) are pedophiles, and clinical sexology and psychiatry have revealed the existence of pedophiles who never commit child sexual offenses.<sup>2</sup> Non-offending pedophiles show better social functioning, greater empathic abilities and greater sexual self-control than pedophilic CSOs.<sup>3</sup>

The available neurobehavioral data from pedophilic CSOs remain widely inconclusive. Typically, general and fronto-temporal neurobiological perturbations appear to be linked to pedophilia and/or child sexual offending.<sup>4</sup> General neurodevelopmental disturbances in pedophilic CSOs are supported by findings of impaired general processing speed, lower general IQ and a higher prevalence of non-right handedness, which suggests disturbed brain lateralization and higher second-to-fourth (2D:4D) digit ratios that indicate lower prenatal androgen exposure.<sup>5</sup> The evidence of reduced cognitive flexibility and lowered inhibitory control abilities in pedophilic CSOs suggests frontal lobe alterations.<sup>4,6</sup> Moreover, lesions in the temporal lobe have been linked to child sexual offending in previously healthy men.<sup>7</sup>

There are six published structural magnetic resonance imaging (MRI) studies on the anatomical features of gray matter in pedophilia that yielded widely inconclusive results.<sup>8–13</sup> In three studies that compared pedophilic CSOs with either healthy controls or other nonsexual offenders, only the reduction in gray matter (GM) in the right amygdala was replicated, whereas differences in the orbitofrontal and prefrontal cortex, striatum, hypothalamus, and the temporal and limbic cortex were inconsistent.<sup>8,9,11</sup> Three studies including pedophiles with and

<sup>1</sup>Division of Forensic Psychiatry, Department of Psychiatry, Psychotherapy and Preventive Medicine, LWL-University Hospital, Bochum, Germany; <sup>2</sup>Institute of Forensic Psychiatry, University of Duisburg-Essen, Duisburg, Germany; <sup>3</sup>Institute of Sexology and Sexual Medicine, Charité—Universitätsmedizin Berlin, Berlin, Germany; <sup>4</sup>Institute of Sexual Medicine and Forensic Psychiatry and Psychotherapy, Medical School, Kiel University, Kiel, Germany; <sup>5</sup>Hannover Medical School, Department of Psychiatry, Hannover, Germany; <sup>6</sup>Division of Mind and Brain Research, Department of Psychiatry and Psychotherapy, Charité—Universitätsmedizin Berlin, Berlin, Germany; <sup>7</sup>Department of Psychiatry, University of Magdeburg, Magdeburg, Germany; <sup>8</sup>Clinical Affective Neuroimaging Laboratory, Department for Behavioral Neurology, Leibniz Institute for Neurobiology, Magdeburg, Germany and <sup>9</sup>Department of Forensic Psychiatry, Psychiatric Hospital of the University of Munich, Munich, Germany. Correspondence: Professor B Schiffer, Division of Forensic Psychiatry, Department of Psychiatry, Psychotherapy and Preventive Medicine, LWL-University Hospital, Alexandrinenstrasse 1-3, 44791 Bochum, Germany. E-mail: boris.schiffer@lwl.org

<sup>10</sup>These authors contributed equally to this work.

Received 30 September 2016; revised 28 March 2017; accepted 29 March 2017

without a history of child sexual offenses identified no reduction in global or regional GM volumes in the pedophilic groups, and in all the studies, the authors did not control for or systematically control for the potentially confounding effects of medication, incarceration and sexual orientation (pedophiles attracted to boys are known to bear a greater risk of re-offending<sup>14</sup>).<sup>10,12,13</sup> Apart from some correlational data, the differential relationship between sexual preference (pedophilia) or offending behavior in pedophilic men and alterations in brain structure thus remain unclear.

The aim of the present study was to overcome the previously mentioned limitations by systematically distinguishing structural brain anomalies associated with pedophilia from those associated with sexual offending in pedophiles. Therefore, we assessed the following three groups of men: (i) pedophilic men who committed sexual offenses against children (P+CSO), (ii) pedophilic men who did not commit sexual offenses against children (P-CSO) and (iii) non-offending teleiophilic (that is, sexually attracted to mature adults) men (HC). Based on the literature, we expected that structural differences within the amygdala would be associated with child sexual offending, pedophilia or other factors, such as incarceration or sexual orientation, that have not been controlled for in the previous studies. Finally, we aimed to analyze structural markers that are potentially related to the risk of re-offending in pedophiles who have already committed offenses against children.

## MATERIALS AND METHODS

### Sample and procedure

From a sample of 244 men that did not fulfill any of the exclusion criteria (see below) and were cross-sectionally recruited at four sites within the NeMUP ([www.nemup.de](http://www.nemup.de)) research collaboration, 58 sexually offending pedophiles (P+CSO, number of victims—Median 2, range 1–60; mean victim age 8.4 years, s.d.=4.0), 60 pedophiles without any contact sexual offenses (P-CSO), and  $N=101$  non-offending teleiophilic men (HC) yielded valid T1-weighted MR-images (also see Supplementary Table 1 for a complete breakdown of the sample distribution across the sites). Twenty-five data sets had to be excluded due to either technical problems in the image acquisition or macroscopic brain pathology. The participants were recruited via online advertisements, forum posts and email lists. The recruitment methods were the same for both pedophilic groups, which additionally but not exclusively comprised participants recruited from legal and clinical institutions, including the 'Prevention Project Dunkelfeld' that offers anonymous treatment for offending and non-offending pedophiles who are currently not under judiciary supervision.<sup>2</sup> The institutional review boards of all the contributing institutions approved the study, and all the participants provided written informed consent. The functional MRI data from an inhibition task completed by parts of the sample have been published elsewhere.<sup>15</sup>

The pedophilic participants fulfilled the diagnostic criteria according to ICD-10. Pedophilia was diagnosed using a guided interview to assess sexual fantasies and behaviors separately. Both fantasies and behaviors were noted on a scale similar to the Kinsey scale for sexual orientation, with the Tanner stages one and five as the poles of the scale (also see the subsection 'Measures').<sup>16</sup> Pedophilia was diagnosed if the participant reported recurrent sexual fantasies involving prepubertal or early pubertal children (Tanner stages one through three) of sufficient intensity to reach orgasm. In the P-CSO group, all the participants reported that immature sexual partners were their preferred sexual fantasy. In the P+CSO group, four participants reported that female partners of Tanner stage four ( $n=2$ ) and five ( $n=2$ ) were their preferred sexual fantasy. Of these participants, an inspection of a viewing reaction time paradigm (see the subsection 'Measures'), self-report or file review data on sexual offenses against children confirmed a pedophilic disorder of sexual preference in two individuals, while the other two individuals were excluded due to diagnostic uncertainty. Of the two retained individuals, one individual reported 'countless' instances of clandestine groping of prepubertal and early pubertal girls in swimming pools, while the other individual reported seven contact sexual offenses against boys aged nine to 12. The viewing reaction time profiles of both offenders showed peak reaction times for the stimuli from the age and gender categories consistent with their offense histories. Child sexual offense was identified whenever an individual

admitted to at least one sexual offense against children under the age of 14, the legal age of consent in Germany, that involved sexually touching or manipulating a child's naked body, penetrating a child or making a child touch or manipulate the offender's genitals or penetrate him. Exhibitionists were excluded from both the pedophilic and teleiophilic groups. For the 14 individuals recruited from prisons, file reviews were used to confirm self-reports.

Sociodemographic, psychopathological and clinical forensic variables were assessed using semi-structured diagnostic interviews (see the subsection 'Measures') conducted by experienced clinicians. Cases presenting any present psychotic, mood or substance use disorder, any severe somatic illness including brain injury and neurological illness, body alterations that could interfere with MRI, or any psychotropic medication, including androgen deprivation therapy, were excluded from the study as well as cases of diagnostic uncertainty regarding pedophilia. Note that under German legislation, pedophiles convicted of child sexual abuse do not necessarily receive medication.<sup>17</sup> All the participants underwent neuropsychological testing as well as an MRI session.

### Measures

The Structured Clinical Interview for the DSM-IV-TR was completed to assess DSM-IV-TR Axis I and II disorders.<sup>18</sup> A semi-structured clinical interview that was developed for the study was conducted to assess pedophilic, hebephilic and other paraphilic sexual interest, sexual and general offense history and the use of child pornography. Sexual orientation and age preference were confirmed with the Kinsey scale,<sup>16</sup> which was extended for the developmental stages of desired sexual partners and a viewing reaction time (VRT) paradigm<sup>19</sup> using the difference between the maximum z-standardized reaction time to images of any mature developmental age category (that is, males or females, Tanner stages four and five) and those to any immature developmental age category (that is, males and females, Tanner stages one through three). Greater values reflected a greater probability of pedophilia according to ICD-10. Global intelligence was estimated from four subtests ('Similarities', 'Vocabulary', 'Block Design' and 'Matrix Reasoning') of the Wechsler Adult Intelligence Scale, 4th Edition.<sup>20</sup> Impulsivity was assessed using the Barratt Impulsiveness Scale (BIS-11).<sup>21</sup> Of the four subscales of the German short version of the Interpersonal Reactivity Index (SPF-IRI), we used perspective taking and empathic concern to characterize the cognitive and affective components of empathic abilities.<sup>22</sup> Sexual inhibition and sexual excitation proneness were assessed using the German version of the SIS/SES questionnaire.<sup>23</sup> Handedness was assessed with the Edinburgh Handedness Inventory.<sup>24</sup> The 2D:4D digit ratio of the right hand was assessed as a proxy for prenatal testosterone exposition and androgenization.<sup>25</sup> We rated the data on committed offenses according to the Screening Scale for Pedophilic Interest, 2nd version (SSPI-2) as a measure of risk of re-offending in pedophilic child molesters.<sup>26,27</sup> In the P+CSO group, the mean SSPI-2 score was 3.6, with a s.d. of 1.2. Further characteristics of the study groups are provided in Table 1.

### Image acquisition and processing

High-resolution T1-weighted images were acquired at four sites on three Siemens Magnetom 3-Tesla scanner types (TimTrio, Skyra and Verio) and one Phillips Achieva 3-Tesla scanner using a magnetization-prepared, rapid gradient-echo (MP-RAGE) sequence (voxel size 1 mm, flip angle 7°, TR 2500 ms, TE 4.33 ms). All images were processed using SPM8 (<http://www.fil.ion.ucl.ac.uk/spm/>) for MATLAB 2011b (MathWorks, Ismaning, Germany). Fluctuations in signals across all sites were controlled for by regularly conducting standardized quality control measurements.<sup>28</sup> The GM was extracted, normalized to a standard template using the 'Diffeomorphic Anatomical Registration using Exponentiated Lie algebra' (DARTEL) algorithm implemented in SPM8, and modulated with normalization parameters to correct for different brain sizes using the VBM8 toolbox (<http://www.neuro.uni-jena.de/vbm/>), which resulted in maps of the individuals' relative GM volumes in voxels that conformed to the Montreal Neurologic Institute space (MNI-space).<sup>29</sup> The images were smoothed with a full-width half maximum kernel of 6 × 6 × 6 mm.

### Statistical analyses

We compared the demographic, forensic, clinical and global brain volume measures of the three groups using one-factorial analysis of variance, Chi-square tests and Kruskal–Wallis tests, which were conducted

**Table 1.** Sample characteristics

	P+CSO (N = 58)	P - CSO (N = 60)	HC (N = 101)	F, $\chi^2$	df	Post hoc comparisons
<i>Sociodemographic characteristics</i>						
Age (M, s.d.)	40.1 (9.1)	34.4 (9.2)	33.8 (10.5)	8.12 <sup>a***</sup>	216, 2	P+CSO > P - CSO P+CSO > HC
In a relationship (N, %)	16 (28)	19 (32)	34 (34)	0.87 <sup>b</sup>	2	—
<i>Educational level</i>						
None to low	20 (35)	3 (5)	7 (7)	41.65 <sup>b***</sup>	4	— P+CSO > P - CSO P+CSO > HC
Trained	23 (40)	20 (33)	26 (26)			—
Higher	15 (26)	37 (61)	68 (67)			P+CSO < P - CSO P+CSO < HC
Unemployed (N, %)	17 (30)	14 (24)	10 (10)	10.29 <sup>b***</sup>	2	P+CSO > HC P - CSO > HC
<i>Clinical and diagnostic characteristics</i>						
WAIS IV score (M, s.d.)	39.8 (9.8)	44.2 (9.1)	43.0 (10.7)	2.97 <sup>a</sup>	213, 2	—
<i>Lifetime DSM-IV-TR diagnoses (N, %)</i>						
Additional axis I disorder	40 (70)	35 (58)	31 (31)	18.27 <sup>b***</sup>	2	P+CSO > HC P - CSO > HC
Alcohol use disorder	12 (24)	6 (10)	6 (6)	10.35 <sup>b**</sup>	2	P+CSO > P - CSO P+CSO > HC
Drug use disorder	3 (6)	4 (7)	2 (2)	2.49 <sup>b</sup>	2	—
Axis II disorder	23 (41)	22 (37)	2 (2)	42.36 <sup>b***</sup>	2	P+CSO > HC P - CSO > HC
Attracted to boys (P)/men (HC) (N, %)	26 (45)	18 (30)	33 (33)	2.15 <sup>b</sup>	2	—
VRT index (M, s.d.)	0.06 (0.51)	0.14 (0.44)	-0.84 (0.54)	93.31 <sup>a***</sup>	214, 2	P+CSO > HC P - CSO > HC
Hebephilic (N, %)	19 (33)	25 (42)	—	1.00 <sup>b</sup>		—
Add. paraphilia <sup>c</sup> (N, %)	13 (29)	12 (20)	14 (14)	5.41 <sup>b</sup>	2	—
No. of nonsexual offenses (median, range)	0 (0-8)	0 (0-2)	0 (0-40)	21.46 <sup>d***</sup>	2	P+CSO > P - CSO P+CSO > HC
CP use (N, %)	44 (73)	41 (68)	0 (0)			
Handedness (EHI)	72.2 (44.8)	65.3 (53.0)	69.2 (51.4)	0.28 <sup>a</sup>	214, 2	—
2D:4D ratio right hand	0.96 (0.04)	0.97 (0.04)	0.99 (0.05)	4.90 <sup>a***</sup>	186, 2	P+CSO < HC
SES (M, s.d.)	51.7 (8.6)	54.9 (7.8)	50.4 (9.1)	5.06 <sup>a***</sup>	207, 2	P - CSO > HC
SIS-1 (M, s.d.)	31.2 (4.8)	31.3 (5.8)	28.5 (5.7)	6.08 <sup>a***</sup>	207, 2	P+CSO > HC P - CSO > HC
SIS-2 (M, s.d.)	27.5 (4.7)	27.0 (5.0)	30.0 (5.7)	7.06 <sup>a***</sup>	207, 2	P+CSO < HC P - CSO < HC
SPF-IRI PT (M, s.d.)	14.1 (2.3)	14.2 (3.0)	14.7 (2.4)	1.10 <sup>a</sup>	205, 2	—
SPF-IRI EC (M, s.d.)	14.5 (3.0)	14.3 (3.3)	14.0 (2.4)	0.45 <sup>a</sup>	205, 2	—
BIS-11 (M, s.d.)	65.2 (9.6)	62.8 (7.8)	61.3 (8.5)	3.54 <sup>a*</sup>	204, 2	P+CSO > HC

Abbreviations: 2D:4D ratio, second-to-fourth digit ratio; CP, child pornography; HC, healthy controls; M, mean; P+CSO, pedophiles with a history of child sexual offending; P - CSO, pedophiles without a history of child sexual offending; SES, sexual excitation scale; SIS-1 sexual inhibition due to threat of performance failure; SIS-2 sexual inhibition due to threat of performance consequences; SPF-IRI, Saarbrücker Persönlichkeitsfragen based on the Interpersonal Reactivity Index scores on perspective taking (PT) and empathic concern (EC); VRT, viewing reaction time (details of the calculation are given in the text); WAIS IV, Wechsler Adult Intelligence Scale, 4th revision. <sup>a</sup>One-way analysis of variance. <sup>b</sup>Pearson's Chi-square; two-sided significance values: \* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ . <sup>c</sup>This measure relates to (additional) paraphilia in terms of a non-pathological form of deviant sexual interest that does not fulfill the criteria for a paraphilic disorder according to DSM-5. <sup>d</sup>Kruskal-Wallis test. Scores of the Short Screening for Pedophilic Interests, Version 2 (SSPI-2) can be calculated for sexual offenders against children only and are thus reported in the text.

in IBM SPSS Statistics Version 22 (IBM, Düsseldorf, Germany and others, 2013).

Using the general linear model, we performed statistical group analyses on the voxel-wise relative GM volumes. Between-group differences in the voxel-wise GM volumes were assessed using two-factorial analysis of covariance (ANCOVA) with group (P+CSO vs P - CSO vs HC) and sexual orientation (attracted to males vs females) as the between-subject factors and acquisition site, age, level of education, verbal IQ and number of nonsexual offenses as nuisance variables. We incorporated sexual orientation as an independent factor to evaluate its influence on group-related GM volume differences and the effect of its interaction with group on GM volume and nonsexual offenses to statistically control for the effects of general criminal behavior. For each contrast, statistical parametric maps were computed to test for differences associated with pedophilia (HC vs P - CSO) or CSO (P - CSO vs P+CSO). To avoid edge effects between the

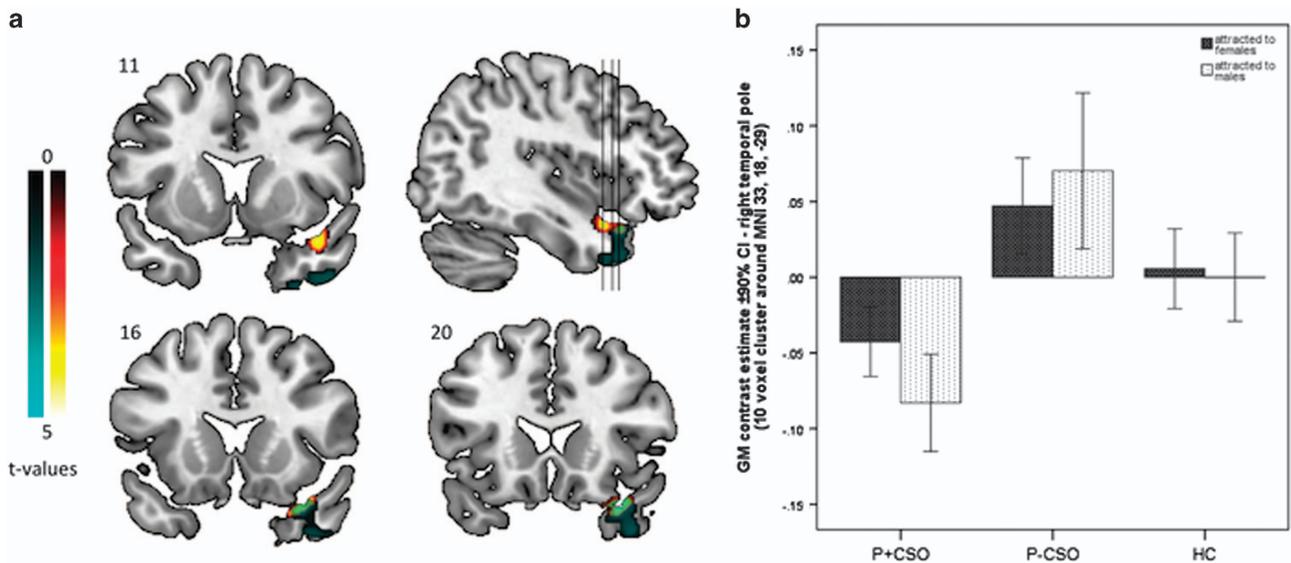
tissue types, we excluded all voxels with relative GM values of less than 0.1 (absolute threshold masking). Owing to the inconsistent results of previous VBM studies in the field, the results of the whole-brain analysis were only considered significant when surviving the conservative threshold of  $P < 0.05$  family-wise error (FWE) that was corrected at the voxel level, that is, every single voxel in the reported clusters exceeded the calculated height threshold.<sup>30</sup>

In the ANCOVA, the assumption of independence of the covariates and the independent variable (in our case group) was not met because the groups differed significantly in age, level of education and verbal IQ. These covariates are also known to affect GM volume and may have removed the variance from the group-factor.<sup>31</sup> Thus, we repeated ANCOVA with a reduced sample of 26P - CSO men, 26P+CSO men and 41 HC men (see Supplementary Table 2), which were carefully matched for age, level of education and verbal IQ. In addition, we took care to include equal

**Table 2.** Global volume measures of the entire sample and matched samples

	<i>P</i> +CSO <i>M</i> ( <i>s.d.</i> )	<i>P</i> −CSO <i>M</i> ( <i>s.d.</i> )	<i>HC</i> <i>M</i> ( <i>s.d.</i> )	<i>F</i>	Post hoc comparisons
<i>Entire sample</i>	<i>N</i> = 58	<i>N</i> = 60	<i>N</i> = 101	<i>df</i> = 216, 2	
TBV	1474.29 (127.30)	1546.80 (113.66)	1539.29 (120.21)	6.84**	<i>P</i> +CSO < <i>P</i> −CSO <i>P</i> +CSO < <i>HC</i>
GM	643.57 (63.00)	693.56 (64.28)	685.28 (57.92)	11.82***	<i>P</i> +CSO < <i>P</i> −CSO <i>P</i> +CSO < <i>HC</i>
GM (adj.) <sup>a</sup>	665.87 (24.10)	680.60 (24.35)	685.28 (27.78)	7.86***	<i>P</i> +CSO < <i>P</i> −CSO <i>P</i> +CSO < <i>HC</i>
WM	569.59 (61.60)	598.39 (55.77)	601.31 (64.45)	5.34**	<i>P</i> +CSO < <i>P</i> −CSO <i>P</i> +CSO < <i>HC</i>
CSF	261.13 (39.76)	254.85 (34.54)	252.70 (41.32)	0.87	
<i>Matched sample</i>	<i>N</i> = 26	<i>N</i> = 26	<i>N</i> = 41	<i>df</i> = 90, 2	
TBV	1482.45 (110.14)	1529.84 (109.01)	1547.95 (129.89)	2.44	—
GM	639.30 (58.70)	674.17 (60.80)	673.16 (57.19)	3.20*	<i>P</i> +CSO < <i>P</i> −CSO <i>P</i> +CSO < <i>HC</i>
GM (adj.) <sup>a</sup>	668.73 (22.84)	669.52 (21.00)	666.86 (26.66)	0.11	—
WM	581.36 (63.75)	592.49 (53.33)	606.59 (67.31)	1.33	—
CSF	261.80 (29.72)	263.19 (39.65)	268.20 (48.01)	0.23	

Abbreviations: CSF, cerebrospinal fluid; GM, gray matter; HC, healthy controls; M, mean; P+CSO, pedophiles with a history of child sexual offending; P−CSO, pedophiles without a history of child sexual offending; TBV, total brain volume; WM, white matter. <sup>a</sup>Adjusted for individual brain size, that is, TBV; \**P* < 0.05; \*\**P* < 0.01; \*\*\**P* < 0.001.



**Figure 1.** (a) Offense-related gray matter (GM) volume reductions were identified using the whole-brain ANCOVA model of both the entire sample (red-colored overlay) and the matched sample (blue-colored overlay) in the right temporal pole, which was superimposed on a standard T1 template that is provided with the MRIcron software. The color bars indicate *t*-statistic values. (b) The bar chart illustrates the contrast estimates of these relative GM volume differences on the single-group level (matched samples) and for the given subgroups attracted to girls/women (white) and boys/men (black), which had no significant impact on the GM volume anomalies in the right temporal pole. All coordinates reference the coordinate system of the Montreal Neurological Institute (MNI). The relative GM volumes were extracted from the modulated, non-adjusted data for the whole clusters. For illustration purposes, the height threshold was set to *P* < 0.001, uncorrected. ANCOVA, analysis of covariance; 90% CI, confidence interval; HC, non-offending teleiophilic men (that is, sexually attracted to adults); P+CSO, pedophilic men who sexually offended against children; P−CSO, pedophilic men who did not sexually offend against children.

numbers of subjects attracted to girls/women or boys/men per group within each acquisition site to avoid systematic biases due to interaction effects of group assignment, sexual orientation and acquisition site. The analysis of the global volume measures and across variables confirmed the successful control of potential confounders (see Table 2).

**Correlational analyses.** To ascertain the relationships between brain volumes that differ between groups and psychological or biological measures that characterize pedophilic child molesters, we extracted the contrast estimates of the brain GM volumes. Using the SPM8 ‘1st eigenvariate’ function, the relative GM volumes in areas that exhibited a significant difference between groups and were adjusted for all the nuisance variables were extracted. Pearson correlations were then calculated between

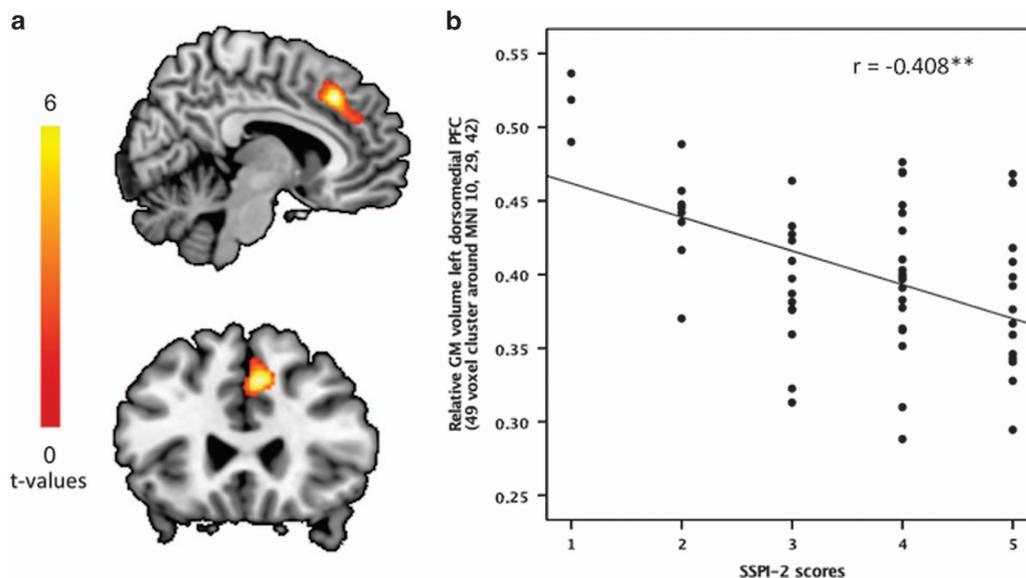
the contrast estimates and the SPF-IRI scores on cognitive and affective empathy, the SIS/SES scores on sexual excitation (SES) and sexual inhibition due to threat of performance failure (SIS-1) and performance consequences (SIS-2), the 2D:4D ratio and the VRT index for both the entire sample and each group separately. We also applied a Bonferroni correction for multiple (that is, 28) comparisons resulting in a corrected threshold of *P* < 0.002.

**Regression analysis.** To analyze the morphometric markers related to the risk of re-offending, regression analysis between the local GM volumes and the SSPI-2 scores was performed within the P+CSO sample (*N* = 58), and we statistically controlled for the effects of the subjects’ age, IQ, education level and acquisition site.

**Table 3.** Correlational analyses

	Contrast estimates GMV right temporal pole (adjusted for age, education, verbal IQ, site and nonsexual offenses)			
	P- CSO	P+CSO	HC	Entire sample
SES	-0.075 (N=59)	0.017 (N=53)	-0.126 (N=98)	-0.029 (N=210)
SIS-1	-0.087 (N=59)	-0.281* (N=53)	-0.256* (N=98)	-0.152* (N=210)
SIS-2	0.244 (*) (N=59)	-0.115 (N=59)	-0.071 (N=98)	0.016 (N=210)
SPF-IRI_PT	0.078 (N=58)	0.038 (N=52)	-0.070 (N=98)	-0.018 (N=208)
SPF-IRI_EC	0.239 (*) (N=58)	-0.048 (N=52)	-0.064 (N=98)	0.010 (N=208)
2D:4D ratio	0.148 (N=46)	-0.220 (N=44)	0.164 (N=95)	0.128 (N=189)
VRT index for pedophilia	0.017 (N=59)	-0.088 (N=58)	-0.202* (N=100)	-0.114 (*) (N=217)

Abbreviations: 2D:4D ratio, second-to-fourth digit ratio; GMV, gray matter volume; HC, healthy controls; IQ, intelligence quotient; P+CSO, pedophiles with a history of child sexual offending; P- CSO, pedophiles without a history of child sexual offending; SES, sexual excitation proneness; SIS-1, sexual inhibition due to threat of performance failure; SIS-2, sexual inhibition proneness due to negative consequences; SPF-IRI, Saarbrücker Persönlichkeitsfragen based on the interpersonal reactivity index scores on perspective taking (PT) and empathic concern (EC); VRT index, viewing reaction time index. Pearson's correlation coefficients. \* $P < 0.05$ ; (\*) $P < 0.10$ .



**Figure 2.** (a) The SSPI-2 score was associated with gray matter (GM) volume differences in the left dorsomedial prefrontal cortex (extending into the dorsal anterior cingulate cortex), which was identified in the whole-brain regression analysis. The color bar indicates t-statistic values and the brain slice at the peak voxel. (b) The scatterplot depicts the linear relationship between the relative GM volume of the left dorsomedial prefrontal cortex and the SSPI-2 scores (Spearman's rho = -0.408,  $P = 0.001$ ). The relative GM volumes were extracted from the modulated, non-adjusted data of the 49 voxels (FWE corrected) clustered around the peak voxel at Montreal Neurological Institute (MNI) 10, 29, 45. For illustration purposes, the height threshold was set to  $P < 0.001$  uncorrected. SSPI-2, Screening Scale for Pedophilic Interest, 2nd version.

## RESULTS

### Voxel-wise group comparisons

Within the first ANCOVA model that comprised the entire sample, the data revealed no regional GM volume differences between the non-offending pedophiles and healthy controls, that is, no pedophilia-only-related anomalies in terms of increased or decreased GM volumes.

However, as depicted in Figure 1a (red-colored overlay), there was a significant difference between the offending and non-offending pedophiles, that is, a CSO-related GM volume reduction that was located in the right temporal pole (TP; Brodmann Area 38; MNI-coordinates of the peak voxel 33; 20; -29; cluster extent ( $k$ ) = 11 voxels;  $T_{\text{peak}} = 5.48$ ;  $df = 206$ ;  $P_{\text{FWE\_peak}} = 0.003$ ). Although the contrast estimates depicted in Figure 1b indicated otherwise,

no significant interaction effect of sexual orientation and CSO was identified in the whole-brain analyses. Nonsignificant results with respect to CSO (that is, given a reduced threshold of  $P < 0.001$  uncorrected on the voxel level and a spatial extent threshold of 45 voxels as calculated according to the theory of Gaussian random fields) were found in the dorsomedial prefrontal cortex (PFC) or dorsal anterior cingulate cortex (ACC), the left ventromedial PFC, the left rostral ACC, the left superior temporal cortex extending into the insular cortex, the right parahippocampal gyrus and the left fusiform gyrus (details are provided in Supplementary Table 3—upper portion).

All results were confirmed within the matched group 'control' analysis, with even stronger statistical support for the CSO-related finding within the right TP (Brodmann Area 38; MNI-coordinates of the peak voxel 33; 20; -29; cluster extent( $k$ ) = 13 voxels;  $T = 5.64$ ;

$df=80$ ;  $P_{FWE\_peak}=0.007$ ; see Figure 1a—blue-colored overlay). There were no other areas of the brain that exhibited significant GM volume differences with the chosen conservative threshold, and the nonsignificant differences (threshold:  $P < 0.001$  uncorrected on the voxel level and an extent threshold of  $k=41$  voxels) resembled those revealed in the entire sample (Supplementary Table 3—lower portion).

#### Correlational analyses

The contrast estimates of the right TP that varied as a function of CSO were negatively correlated with the SIS-1 scores in the P+CSO, HC and the entire sample; there was also a negative correlation between the contrast estimates and the VRT index in HC. In the non-offending pedophiles, the SIS-2 scores and the SPF-IRI empathic concern showed a trend toward a significant positive correlation with the right TP volume. However, none of these correlations survived the correction for multiple comparisons (see Table 3).

#### Regression analysis

The regional GM volume was significantly negatively associated with the SSPI-2 scores in the right dorsomedial prefrontal cortex, which extended into the right dorsal anterior cingulate cortex (MNI-coordinates: 10; 29; 42 cluster extent( $k$ )=49 voxels;  $T=5.74$ ;  $P_{FWE\_peak}=0.008$ ), that is, the lower volume in this area, the higher the risk of re-offending (Spearman's  $\rho=-0.408$ ;  $P=0.001$ ; see Figure 2).

#### Post hoc analyses

Contradicting our hypotheses, the whole-brain analyses failed to confirm a pedophilia- or a CSO-related GM volume deficit in the right amygdala. Thus, we performed a regions of interest analysis (using the Wake Forest University PickAtlas Tool and Aal atlas and the second ANCOVA model covering the matched sample) on the right amygdala to explore whether the prior findings may be explained by the fact that CSOs, who are mostly attracted to boys, have been compared with controls, who are mostly attracted to adult women.<sup>9,11</sup> As shown in Supplementary Figure 1, we found a significant GM volume reduction in the right amygdala of the P+CSO only when we directly compared the P+CSO attracted to boys and HC attracted to women (MNI-coordinates of the peak voxel 21; 2; -20; cluster extent( $k$ )=48 voxels;  $T=4.24$ ;  $df=80$ ;  $P_{FWE} < 0.05$ ).

## DISCUSSION

To the best of our knowledge, this is the first study to differentiate brain structural anomalies in pedophiles with and without a history of CSO. Consistent with the conceptualization of the DSM-5, which specifies CSO as most the prominent criterion that differentiates pedophilia from pedophilic disorder, there were no significant differences between the GM volumes of the non-offending pedophiles and the teleiophilic controls. In contrast, the pedophiles who had engaged in CSO showed a significantly reduced relative GM volume in the right TP compared with pedophiles who did not. This difference was not attributable to age, level of education, IQ, sexual orientation, drug misuse/dependence, other Axis I or II disorders or general criminality. However, the GM volume in the right TM was negatively associated with self-focused sexual behavior in both healthy controls and offending pedophiles and the VRT index, which is a measure of pedophilic tendencies in healthy controls. Moreover, the GM volume in the right TM was positively correlated with affective empathic skills and the propensity to inhibit sexual behavior due to potentially negative consequences of sex in non-offending pedophiles. Finally, the risk of re-offending, which was

predicted by the SSPI-2 scores, was significantly associated with decreased local GM volume in the right dorsomedial PFC/ACC.

The pattern of above vs below 'normal' GM volume of the right TP of the non-offending vs offending pedophiles potentially suggests that the risk for CSO in pedophiles is modulated by GM volume or the function of this area. Supporting this notion, the development of Klüver–Bucy syndrome in men and in nonhuman primates following lesions in the TP is characterized by impairments in deciphering social cues and sexual disinhibition.<sup>32</sup> In functional MRI research, this finding is also supported by evidence showing that TP deactivation is a precondition for sexual response to visual sexual stimuli and activation in theory of mind and empathy.<sup>33,34</sup> The location in the temporal pole region does not readily connect to the findings associated with antisociality/psychopathy, which are pathologies that are also characterized by a lack of empathy and high sexual behavioral output but are typically associated with prefrontal and limbic gray matter deficits.<sup>35</sup> One finding of interest may be the apparent differential distribution (CSO by sexual orientation interaction) of the relative GM volume in the right TP with respect to sexual orientation. Although this association was not statistically significant, there is a more pronounced reduction in GM in pedophiles who are attracted to boys, which is consistent with the literature showing this population is at greater risk for committing multiple contact sexual offenses. The pattern of correlations in our study lends further support to an interpretation of these findings that is specific for pedophilic sexual offending. The items pertaining to the SIS-1 mainly represent self-focus in sexual behavior. This association with self-focus in offending pedophiles and healthy controls contrasts with an inverse association with measures of other-focused tendencies, such as empathic concern and sexual inhibition due to performance consequences in pedophilic non-offenders. The divergence between the three groups may be driven by some latent function that differentially influences response behavior and helps non-offending pedophiles to abstain from contact sexual offending. However, caution in the interpretation of these associations is warranted, as the SIS/SES questionnaire has not yet been validated in pedophilic samples. The association between reduced TP volume and increased pedophilic response behavior in an indirect measure of sexual preference in healthy controls is intriguing and may indicate a finding relevant to the etiology of pedophilia.

In our study, the GM volume in the dorsomedial PFC/ACC was negatively correlated with a quantitative marker for pedophilia that is associated with the risk to re-offend (SSPI-2). This finding is related to antisociality and contributes to the existing literature on the deficient inhibitory control in pedophilic CSOs. The dorsomedial PFC/ACC is the key area involved in the cognitive behavioral control processes, including conflict monitoring and the mediation of conflicts between the emotional and rational components of moral judgement, which is related to violent behavior.<sup>35–37</sup>

In contrast to prior work, there were no GM volume differences between the groups in the right amygdala.<sup>9,11</sup> However, as indicated by our *post hoc* analysis, the previously reported differences may be due to unbalanced group designs regarding sexual orientation, although the research thus far has failed to establish clear-cut neuroanatomical differences between teleiophilic men attracted to men or women.<sup>38</sup> Nonetheless, an automated study of the amygdala volume using VBM is prone to error, and studies using other methodologies, such as manual volumetry, are needed to confirm this finding.

#### Limitations

The cross-sectional design of this study impedes causal explanations or predictive interpretations of the between-group differences. Moreover, the differences in the white matter and the gray matter, which can be detected with other methods, are possible

and may add to the results of our study. As a third methodological concern, more effective methods to control for the influence of MRI analyses than regression modeling have been proposed.<sup>39</sup> Given that our finding held in the matched group analysis with a well-balanced group distribution between the sites (see Supplementary Table 1), a bias introduced through the different acquisition sites appears unlikely.

Recruiting pedophiles from the community to distinguish between pedophilia and CSO is a major strength but also a limitation because evidence for or against self-reported offenses is unavailable. However, the probability that some participants in the P–CSO group may have falsely denied sexual offenses seems to be rather small due to the clear-cut findings, guaranteed confidentiality of all information and the possibility of anonymous participation. A similar argument can be made for the influence of Axis I or II disorders. Although our model did not allow for the clarification of the influence of Axis I or II disorders on the GM differences, the pedophilic groups did not significantly differ in their psychiatric comorbidities, which indicates that these issues were unlikely to contribute to the difference in the GM volume in the temporal pole. The proportions of the 'classic' pedophilic and hebephilic (attracted to early pubescent rather than strictly prepubescent children) men were similar within both pedophilic groups and therefore probably did not affect the between-group differences detected in this study. However, the similar proportions may have diluted differences between these groups and the teleiophilic group; one study demonstrated that the white matter differences between hebephilic and teleiophilic men were smaller than those between pedophilic and teleiophilic men.<sup>40</sup> In addition, the lack of clear correlations between the TP volume and psychological or behavioral measures does impede the direct application of this result to therapeutic approaches. Further studies are needed to elucidate this connection. Finally, while the results of the current study are valid for pedophilic CSOs, the generalizability of these findings to non-pedophilic child molesters should be addressed in other studies.

## CONCLUSION

The present study substantiates the idea that CSO in pedophilia rather than pedophilia alone is associated with changes in GM integrity, particularly in the right temporal pole. The risk of (re)offending was associated with a GM reduction in the dorsomedial PFC/ACC. Both findings indicate that morphometric markers associated with CSO in pedophiles may be potentially useful for the treatment or prevention approaches that aim to reduce the risk of (re)offending in pedophilia.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## ACKNOWLEDGMENTS

This research is part of a multisite research project on the neural mechanisms underlying pedophilia and sexual offending against children (called NeMUP), which is funded by the Federal Ministry of Education and Research (BMBF): 01KR1205 to BS, MW, KMB, HW, JP and THCK. The study was also funded by the German Research Foundation (DFG): Schi 1034/3-1 to BS.

## REFERENCES

- Dombert B, Schmidt AF, Banse R, Briken P, Hoyer J, Neutze J et al. How common is males' self-reported sexual interest in prepubescent children? *J Sex Res* 2016; **53**: 214–223.
- Beier KM, Neutze J, Mundt IA, Ahlers CJ, Goecker D, Konrad A et al. Encouraging self-identified pedophiles and hebephiles to seek professional help: first results of the Prevention Project Dunkelfeld (PPD). *Child Abuse Negl* 2009; **33**: 545–549.
- Cantor JM, McPhail IV. Non-offending pedophiles. *Curr Sex Health Rep* 2016; **8**: 1–8.
- Tenbergen G, Wittfoth M, Frieling H, Ponseti J, Walter M, Walter H et al. The neurobiology and psychology of pedophilia: recent advances and challenges. *Front Hum Neurosci* 2015; **9**: 344.
- Blanchard R, Cantor JM, Robichaud LK. Biological factors in the development of sexual deviance and aggression in males. In: Barbaree HE, Marshall WL (eds). *The Juvenile Sex Offender*. Guilford Press: New York, NY, USA, 2008, pp 77–105.
- Joyal CC, Black DN, Dassylva B. The neuropsychology and neurology of sexual deviance: a review and pilot study. *Sex Abuse J Res Treat* 2007; **19**: 155–173.
- Mohnke S, Müller S, Amelung T, Krüger THC, Ponseti J, Schiffer B et al. Brain alterations in paedophilia: a critical review. *Prog Neurobiol* 2014; **122**: 1–23.
- Schiffer B, Peschel T, Paul T, Gizewski E, Forsting M, Leygraf N et al. Structural brain abnormalities in the frontostriatal system and cerebellum in pedophilia. *J Psychiatr Res* 2007; **41**: 753–762.
- Schiltz K, Witzel J, Northoff G, Zierhut K, Gubka U, Fellmann H et al. Brain pathology in pedophilic offenders: evidence of volume reduction in the right amygdala and related diencephalic structures. *Arch Gen Psychiatry* 2007; **64**: 737.
- Cantor JM, Kabani N, Christensen BK, Zipursky RB, Barbaree HE, Dickey R et al. Cerebral white matter deficiencies in pedophilic men. *J Psychiatr Res* 2008; **42**: 167–183.
- Poepl TB, Nitschke J, Santtila P, Schecklmann M, Langguth B, Greenlee MW et al. Association between brain structure and phenotypic characteristics in pedophilia. *J Psychiatr Res* 2013; **47**: 678–685.
- Gerwin H, Pohl A, Granert O, van Eimeren T, Wolff S, Jansen O et al. The (in) consistency of changes in brain macrostructure in male paedophiles: a combined T1-weighted and diffusion tensor imaging study. *J Psychiatr Res* 2015; **68**: 246–253.
- Cantor JM, Lafaille S, Soh DW, Moayed M, Mikulis DJ, Girard TA. Diffusion tensor imaging of pedophilia. *Arch Sex Behav* 2015; **44**: 2161–2172.
- Seto MC, Harris GT, Rice ME, Barbaree HE. The screening scale for pedophilic interests predicts recidivism among adult sex offenders with child victims. *Arch Sex Behav* 2004; **33**: 455–466.
- Kärgel C, Massau C, Weiß S, Walter M, Borchardt V, Krüger THC et al. Evidence for superior neurobiological and behavioral inhibitory control abilities in non-offending as compared to offending pedophiles. *Hum Brain Mapp* 2016; **38**: 1092–1104.
- Kinsey AC, Pomeroy WB, Martin CE. *Sexual Behavior in the Human Male*. Indiana University Press: Bloomington, IN, USA, 1975.
- Briken P, Welzel K, Habermann N, Hill A, Berner W. Antiandrogene Therapie und Lockerungen bei Sexualstraf Tätern im Maßregelvollzug Berlin. [Antiandrogenic pharmacotherapy of sexual offenders and home leave steps in the forensic psychiatric hospital Berlin]. *Psychiatr Prax* 2009; **36**: 232–237.
- Wittchen H-U, Zaudig M, Fydrich T. *Strukturiertes Klinisches Interview für DSM-IV Achse I & II*. Hogrefe: Göttingen, Germany, 1997.
- Imhoff R, Schmidt AF, Nordsiek U, Luzar C, Young AW, Banse R. Viewing time effects revisited: prolonged response latencies for sexually attractive targets under restricted task conditions. *Arch Sex Behav* 2010; **39**: 1275–1288.
- Wechsler D. *Wechsler Adult Intelligence Scale - Third Edition (WAIS-III)*. The Psychological Corporation: San Antonio, TX, USA, 1997.
- Preuss UW, Rujescu D, Giegling I, Watzke S, Koller G, Zetzsche T et al. Psychometrische evaluation der deutschsprachigen Version der Barratt-Impulsivness-Skala. *Nervenarzt* 2008; **79**: 305–319.
- Paulus C. Der Saarbrücker Persönlichkeitsfragebogen SPF (IRI) zur Messung von Empathie. Psychometrische Evaluation der deutschen Version des Interpersonal Reactivity Index 2009. Available at <http://hdl.handle.net/20.500.11780/3343> (accessed 16 March 2011).
- Janssen E, Vorst H, Finn P, Bancroft J. The Sexual Inhibition (SIS) and Sexual Excitation (SES) Scales: I. Measuring sexual inhibition and excitation proneness in men. *J Sex Res* 2002; **39**: 114–126.
- Oldfield RC. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* 1971; **9**: 97–113.
- Hönekopp J, Bartholdt L, Beier L, Liebert A. Second to fourth digit length ratio (2D:4D) and adult sex hormone levels: new data and a meta-analytic review. *Psychoneuroendocrinology* 2007; **32**: 313–321.
- Seto MC, Stephens S, Lalumière ML, Cantor JM. The revised screening scale for pedophilic interests (SSPI-2) development and criterion-related validation. *Sex Abuse J Res Treat*; e-pub ahead of print 20 November 2015; doi: 10.1177-/1079063215612444.
- Seto MC, Sandler JC, Freeman NJ. The revised screening scale for pedophilic interest: predictive and concurrent validity. *Sex Abuse J Res Treat*; e-pub ahead of print 16 December 2015; doi: 1079/063215618375.
- Hellerbach A, Schuster V, Jansen A, Sommer J. MRI phantoms—are there alternatives to agar. *PLoS ONE* 2013; **8**: e70343.

- 29 Ashburner J. A fast diffeomorphic image registration algorithm. *Neuroimage* 2007; **38**: 95–113.
- 30 Eklund A, Nichols TE, Knutsson H. Cluster failure: why fMRI inferences for spatial extent have inflated false-positive rates. *Proc Natl Acad Sci USA* 2016; **113**: 7900–7905.
- 31 Miller GA, Chapman JP. Misunderstanding analysis of covariance. *J Abnorm Psychol* 2001; **110**: 40–48.
- 32 Devinsky J, Sacks O, Devinsky O. Klüver–Bucy syndrome, hypersexuality, and the law. *Neurocase* 2010; **16**: 140–145.
- 33 Lamm C, Decety J, Singer T. Meta-analytic evidence for common and distinct neural networks associated with directly experienced pain and empathy for pain. *Neuroimage* 2011; **54**: 2492–2502.
- 34 Stoleru S, Fonteille V, Cornélis C, Joyal C, Moulier V. Functional neuroimaging studies of sexual arousal and orgasm in healthy men and women: a review and meta-analysis. *Neurosci Biobehav Rev* 2012; **36**: 1481–1509.
- 35 Glenn AL, Johnson AK, Raine A. Antisocial personality disorder: a current review. *Curr Psychiatry Rep* 2013; **15**: 427.
- 36 Ridderinkhof KR. The role of the medial frontal cortex in cognitive control. *Science* 2004; **306**: 443–447.
- 37 Greene JD, Nystrom LE, Engell AD, Darley JM, Cohen JD. The neural bases of cognitive conflict and control in moral judgment. *Neuron* 2004; **44**: 389–400.
- 38 Bailey JM, Vasey PL, Diamond LM, Breedlove SM, Vilain E, Epprecht M. Sexual orientation, controversy, and science. *Psychol Sci Public Interest* 2016; **17**: 45–101.
- 39 Moorhead TWJ, Gountouna VE, Job DE, McIntosh AM, Romaniuk L, Lymer GKS *et al*. Prospective multicentre Voxel Based Morphometry study employing scanner specific segmentations: procedure development using CaliBrain structural MRI data. *BMC Med Imaging* 2009; **9**: 8.
- 40 Cantor JM, Blanchard R. White matter volumes in pedophiles, hebephiles, and teleiophiles. *Arch Sex Behav* 2012; **41**: 749–752.



This work is licensed under a Creative Commons Attribution-NonCommercial-NoDerivs 4.0 International License. The images or other third party material in this article are included in the article's Creative Commons license, unless indicated otherwise in the credit line; if the material is not included under the Creative Commons license, users will need to obtain permission from the license holder to reproduce the material. To view a copy of this license, visit <http://creativecommons.org/licenses/by-nc-nd/4.0/>

© The Author(s) 2017

Supplementary Information accompanies the paper on the Translational Psychiatry website (<http://www.nature.com/tp>)